

Claims

1. A method of separating a target biological material from a mixture, said method comprising the step of contacting said mixture with a superparamagnetic polysaccharide matrix in an aqueous solution having a pH of between 3 and 10, wherein said superparamagnetic polysaccharide matrix is prepared by a method comprising the steps of:

(a) diffusing an Fe(II) salt into said polysaccharide matrix, thereby entrapping Fe(II) ions within the matrix; and

(b) oxidizing said entrapped Fe(II) ions with nitrate under alkaline conditions to convert said Fe(II) ions into superparamagnetic ferric oxide particles.

2. The method of claim 1, wherein said polysaccharide is starch, cross-linked starch, chitosan, chitin crystallites, dextran, cross-linked dextran, cellulose, cellulose fibers, microcrystalline cellulose, alginic acid, hyaluronic acid, glycogen, or a glycosylaminoglycan.

3. The method of claim 2, wherein said polysaccharide is cross-linked starch, cross-linked dextran, chitosan, chitin crystallites, microcrystalline cellulose, or cellulose fibers.

4. The method of claim 1, wherein said superparamagnetic polysaccharide matrix further comprises a ligand having affinity for said target biological material.

5. The method of claim 4, wherein said ligand is covalently attached to said polysaccharide matrix.

6. The method of claim 5, wherein said ligand comprises a protein, a peptide, a carbohydrate, a glycopeptide, a glycoprotein, a glycosylaminoglycan, a cationic lipid, a glycolipid, or a polynucleotide.

7. The method of claim 6, wherein said ligand is protein A.

8. The method of claim 1, wherein said polysaccharide matrix further comprises charged groups.

9. The method of claim 8, wherein said charged groups are selected from carboxyl, ammonium, sulfate, or combinations thereof.

10. The method of claim 9, wherein polysaccharide matrix comprises between 1 and 200 mole percent carboxyl groups per saccharide unit.

11. The method of claim 1, wherein said target biological material is selected from protozoa, bacteria, fungi, yeast, cultured cells from multicelled organisms, viruses, organelles, suborganelles, proteins, glycoproteins, vaccines, lipoproteins, carbohydrates, lipids, and fragments thereof.

12. The method of claim 11, wherein said target biological material is a protein.

13. The method of claim 12, wherein said protein is selected from antibodies, albumins, angiogenic factors, antibodies, clotting factors, colony stimulating factors, cytokines, differentiation factors, enzymes, growth factors, growth hormones, immune globulins, interferons, interleukins, poietins, somatotropin-releasing hormones, and tachykinins.

14. The method of claim 13, wherein said protein is an antibody selected from trastuzumab, oprelvekin, muromonab-CD3, infliximab, abciximab, ritiximab, basiliximab, palivizumab, cetuximab, daclizumab, and antibodies to immune globulins.

15. The method of claim 12, wherein said protein is selected from antihemophilic factor, bactericidal/permeability increasing protein rBPI-21, calcitonin, ceredase, factor IV, factor VIII, factor IX, factor VIIa, GM-CSF, G-CSF, TNF-alpha, interferon alpha, interferon beta, interferon gamma, RNases, DNases, proteases, urate oxidase, adenosine deaminase, alronidase, alpha galactosidase, alpha glucosidase, vascular endothelial growth factor, endothelial cell growth factor, epidermal growth factor, basic fibroblast growth factor, and platelet derived growth factor, human growth hormone, bovine growth hormone, fibrin, follicle-stimulating hormone, glucocere-brosidase, herudin, antithymocyte globulin, hepatitis B immune globulin, CMV immune globulin, insulin, interleukin-2, interleukin-11, leptin, luteinizing hormone (LH), osteogenic protein-1, osteoprotegerin, platelet activating factor-acetylhydrolase (rPAF-AH), parathyroid hormone, erythropoietin, thrombopoietin, prolactin, relaxin, RSV, thyroid-stimulating hormone, thyrotropin alfa, rhIGF-I/rhIGFBP-3 complex, LFA-3/IgG1 human fusion protein, and tissue plasminogen activator.

16. The method of claim 1, wherein the pH of said mixture is between 5 and 8.

17. The method of claim 1, wherein said contacting is performed in the presence of a buffer.

18. The method of claim 17, wherein said buffer is selected from acetate, citrate, phosphate, tris(hydroxymethyl)amino methane (Tris), glycine, carbonate, lactate, pivalate, pyridine, picolinate, succinate, histidine, N-Morpholinosulfonic acid (Mes), Bis-(-2-hydroxyethyl)imino-tris-(hydroxymethyl)methane, (Bis-Tris), N-(2-acetamido)-2-aminoethane sulfonic acid (Aces), imidazole, N-morpholinopropane sulfonic acid (Mops), N-tris(hydroxymethyl)methyl-2-aminoethane sulfonic acid (Tes), triethanolamine, N-tris(hydroxymethyl)methyl-glycine (Tricine), tris(hydroxymethyl)aminopropane sulfonic acid (Taps), 2-amino-2-methyl-1,3-propanediol, diethanolamine, taurine, ammonia, borate, ethanolamine, aminopropan-3-ol, and combinations thereof.

19. The method of claim 1, further comprising the step of rinsing said target biological material from said matrix using a solution of high conductivity.

20. The method of claim 1, wherein said mixture comprises between 10 mg/L and 5g/L target biological material.

21. The method of claim 20, wherein said mixture comprises between 500 mg/L and 3 g/L target biological material.

22. The method of claim 1, wherein said mixture comprises an unclarified fermentation broth or cell lysate.

23. The method of claim 1, wherein said mixture is clarified prior to contacting said matrix.

24. The method of claim 1, further comprising the step of applying a magnetic field to said mixture after said contacting.

25. The method of claim 1, wherein said contacting occurs during a packed bed chromatographic separation.

26. The method of claim 1, wherein said contacting occurs during an expanded bed adsorption separation.

27. A composition comprising a polysaccharide matrix having charged groups selected from carboxyl, ammonium, sulfate, or combinations thereof, and a superparamagnetic iron oxide particle within said matrix, wherein said composition is prepared by a method comprising the steps of:

- (a) diffusing an Fe(II) salt into a matrix, thereby entrapping Fe(II) ions within the matrix; and
- (b) oxidizing said entrapped Fe(II) ions with nitrate under alkaline conditions to convert said Fe(II) ions into superparamagnetic ferric oxide particles.

28. The composition of claim 27, wherein said polysaccharide matrix comprises cellulose and said charged group is carboxyl.

29. The composition of claim 27, wherein said polysaccharide matrix comprises starch and said charged group is ammonium.

30. The composition of claim 27, wherein said polysaccharide matrix comprises chitosan and said charged group is ammonium.

31. The composition of claim 27, wherein said polysaccharide matrix comprises chitosan and said charged group is sulfate.